

Please replace the subtitle on Page 76, line 11, following the second paragraph with:

- - EXAMPLE 6: DIMERIZATION OF PHOSPHORYLATED STAT91 - -

Please amend the title of the application to read:

- - NUCLEIC ACIDS ENCODING RECEPTOR RECOGNITION FACTORS  
AND METHODS OF USE THEREOF - -

Applicants request that the Specification be amended to include the Sequence Listing submitted herewith.

IN THE CLAIMS:

Please cancel Claims 2-68 without prejudice:

Please add the following new claims.

--69. A recombinant DNA molecule encoding a receptor recognition factor (RRF) protein having the following characteristics:

- a) said RRF is cytoplasmic in origin;
- b) said RRF is activated by tyrosine phosphorylation;
- c) upon activation said RRF is translocated to the nucleus of a target cell; and
- d) said RRF has an amino acid sequence comprising a sequence of contiguous amino acid residues which is present in both SEQ ID NO:2 and SEQ ID NO:4; wherein the sequence of contiguous amino acid residues contains four or more consecutive amino acids.

70. The recombinant DNA molecule of Claim 69 wherein the sequence of contiguous amino acid residues contains four or more consecutive amino acids and is selected from the group consisting of:

- a) HQLY (amino acids 19-22 of SEQ ID NO:2 and 19-22 of SEQ ID NO4);
- b) IRQY (amino acids 31-34 of SEQ ID NO:2 and 30-33 of SEQ ID NO4);
- c) RQYL (amino acids 32-35 of SEQ ID NO:2 and 31-34 of SEQ ID NO4);
- d) LLQH (amino acids 82-85 of SEQ ID NO:2 and 78-81 of SEQ ID NO4);
- e) LQHN (amino acids 83-86 of SEQ ID NO:2 and 79-82 of SEQ ID NO4);

- f) RKEV (amino acids 210-213 of SEQ ID NO:2 and 210-213 of SEQ ID NO:4);
- g) FVVE (amino acids 316-319 of SEQ ID NO:2 and 317-320 of SEQ ID NO:4);
- h) QPCM (amino acids 321-324 of SEQ ID NO:2 and 322-325 of SEQ ID NO:4);
- i) PCMP (amino acids 322-325 of SEQ ID NO:2 and 323-326 of SEQ ID NO:4);
- j) LKTG (amino acids 334-337 of SEQ ID NO:2 and 335-338 of SEQ ID NO:4);
- k) RLLV (amino acids 345-348 of SEQ ID NO:2 and 346-349 of SEQ ID NO:4);
- l) GFRK (amino acids 372-375 of SEQ ID NO:2 and 376-379 of SEQ ID NO:4);
- m) FRKF (amino acids 373-376 of SEQ ID NO:2 and 377-380 of SEQ ID NO:4);
- n) RKFN (amino acids 374-377 of SEQ ID NO:2 and 378-381 of SEQ ID NO:4);
- o) KFNI (amino acids 375-378 of SEQ ID NO:2 and 379-382 of SEQ ID NO:4);
- p) FNIL (amino acids 376-379 of SEQ ID NO:2 and 380-383 of SEQ ID NO:4);
- q) VTEE (amino acids 424-427 of SEQ ID NO:2 and 426-429 of SEQ ID NO:4);
- r) TEEL (amino acids 425-428 of SEQ ID NO:2 and 427-430 of SEQ ID NO:4);
- s) EELH (amino acids 426-429 of SEQ ID NO:2 and 428-431 of SEQ ID NO:4);
- t) LPVV (amino acids 451-454 of SEQ ID NO:2 and 453-456 of SEQ ID NO:4);
- u) LSWQ (amino acids 500-503 of SEQ ID NO:2 and 502-505 of SEQ ID NO:4);
- v) SWQF (amino acids 501-504 of SEQ ID NO:2 and 503-506 of SEQ ID NO:4);
- w) WQFS (amino acids 502-505 of SEQ ID NO:2 and 504-507 of SEQ ID NO:4);
- x) QFSS (amino acids 503-506 of SEQ ID NO:2 and 505-508 of SEQ ID NO:4);
- y) RGLN (amino acids 510-513 of SEQ ID NO:2 and 512-515 of SEQ ID NO:4);
- z) ILEL (amino acids 560-563 of SEQ ID NO:2 and 561-564 of SEQ ID NO:4);
- zz) LWND (amino acids 571-574 of SEQ ID NO:2 and 572-575 of SEQ ID NO:4);
- aa) WNDG (amino acids 572-575 of SEQ ID NO:2 and 573-576 of SEQ ID NO:4);
- bb) IMGF (amino acids 577-580 of SEQ ID NO:2 and 578-581 of SEQ ID NO:4);
- cc) GTFL (amino acids 596-599 of SEQ ID NO:2 and 597-600 of SEQ ID NO:4);
- dd) TFLI (amino acids 597-600 of SEQ ID NO:2 and 598-601 of SEQ ID NO:4);
- ee) FLLR (amino acids 598-601 of SEQ ID NO:2 and 599-602 of SEQ ID NO:4);
- ff) LLRF (amino acids 599-602 of SEQ ID NO:2 and 600-603 of SEQ ID NO:4);
- gg) LRFS (amino acids 600-603 of SEQ ID NO:2 and 601-604 of SEQ ID NO:4);
- hh) RFSE (amino acids 601-604 of SEQ ID NO:2 and 602-605 of SEQ ID NO:4);

- ii) FSES (amino acids 602-605 of SEQ ID NO:2 and 603-606 of SEQ ID NO:4);
- jj) SESS (amino acids 603-606 of SEQ ID NO:2 and 604-607 of SEQ ID NO:4);
- kk) PYTK (amino acids 630-633 of SEQ ID NO:2 and 633-636 of SEQ ID NO:4);
- ll) ENIP (amino acids 654-657 of SEQ ID NO:2 and 657-660 of SEQ ID NO:4);
- mm) NIPE (amino acids 655-658 of SEQ ID NO:2 and 658-661 of SEQ ID NO:4);
- nn) IPEN (amino acids 656-659 of SEQ ID NO:2 and 659-662 of SEQ ID NO:4);
- oo) PENP (amino acids 657-660 of SEQ ID NO:2 and 660-663 of SEQ ID NO:4); and
- pp) ENPL (amino acids 658-661 of SEQ ID NO:2 and 661-664 of SEQ ID NO:4).

71. The recombinant DNA molecule of Claim 70 wherein the sequence of contiguous amino acid residues contains five or more consecutive amino acids and is selected from the group consisting of:

- a) IRQYL (amino acids 31-35 of SEQ ID NO:2 and 30-34 of SEQ ID NO:4);
- b) LLQHN (amino acids 82-86 of SEQ ID NO:2 and 78-82 of SEQ ID NO:4);
- c) QPCMP (amino acids 321-325 of SEQ ID NO:2 and 322-326 of SEQ ID NO:4);
- d) GFRKF (amino acids 372-376 of SEQ ID NO:2 and 376-380 of SEQ ID NO:4);
- e) FRKFN (amino acids 373-377 of SEQ ID NO:2 and 377-381 of SEQ ID NO:4);
- f) RKFNI (amino acids 374-378 of SEQ ID NO:2 and 378-382 of SEQ ID NO:4);
- g) KFNIL (amino acids 375-379 of SEQ ID NO:2 and 379-383 of SEQ ID NO:4);
- h) VTEEL (amino acids 424-428 of SEQ ID NO:2 and 426-430 of SEQ ID NO:4);
- i) TEELH (amino acids 425-429 of SEQ ID NO:2 and 427-431 of SEQ ID NO:4);
- j) LSWQF (amino acids 500-504 of SEQ ID NO:2 and 502-506 of SEQ ID NO:4);
- k) SWQFS (amino acids 501-505 of SEQ ID NO:2 and 503-507 of SEQ ID NO:4);
- l) WQFSS (amino acids 502-506 of SEQ ID NO:2 and 504-508 of SEQ ID NO:4);
- m) LWNDG (amino acids 571-575 of SEQ ID NO:2 and 572-576 of SEQ ID NO:4);
- n) GTFLL (amino acids 596-600 of SEQ ID NO:2 and 597-601 of SEQ ID NO:4);
- o) TFLLR (amino acids 597-601 of SEQ ID NO:2 and 598-602 of SEQ ID NO:4);
- p) FLLRF (amino acids 598-602 of SEQ ID NO:2 and 599-603 of SEQ ID NO:4);
- q) LLRFS (amino acids 599-603 of SEQ ID NO:2 and 600-604 of SEQ ID NO:4);
- r) LRFSE (amino acids 600-604 of SEQ ID NO:2 and 601-605 of SEQ ID NO:4);

- s) RFSES (amino acids 601-605 of SEQ ID NO:2 and 602-606 of SEQ ID NO:4);
- t) FSESS (amino acids 602-606 of SEQ ID NO:2 and 603-607 of SEQ ID NO:4);
- u) ENIPE (amino acids 654-658 of SEQ ID NO:2 and 657-661 of SEQ ID NO:4);
- v) NIPEN (amino acids 655-659 of SEQ ID NO:2 and 658-662 of SEQ ID NO:4);
- w) IPENP (amino acids 656-660 of SEQ ID NO:2 and 659-663 of SEQ ID NO:4); and
- x) PENPL (amino acids 657-661 of SEQ ID NO:2 and 660-664 of SEQ ID NO:4).

72. The recombinant DNA molecule of Claim 71 wherein the sequence of contiguous amino acid residues contains six or more consecutive amino acids and is selected from the group consisting of:

- a) GFRKFN (amino acids 372-377 of SEQ ID NO:2 and 376-381 of SEQ ID NO:4);
- b) FRKFNI (amino acids 373-378 of SEQ ID NO:2 and 377-382 of SEQ ID NO:4);
- c) RKFNIL (amino acids 374-379 of SEQ ID NO:2 and 378-383 of SEQ ID NO:4);
- d) VTEELH (amino acids 424-429 of SEQ ID NO:2 and 426-431 of SEQ ID NO:4);
- e) LSWQFS (amino acids 500-505 of SEQ ID NO:2 and 502-507 of SEQ ID NO:4);
- f) SWQFSS (amino acids 501-506 of SEQ ID NO:2 and 503-508 of SEQ ID NO:4);
- g) GTFLLR (amino acids 596-601 of SEQ ID NO:2 and 597-602 of SEQ ID NO:4);
- h) TFLLR (amino acids 597-602 of SEQ ID NO:2 and 598-603 of SEQ ID NO:4);
- i) FLLRFS (amino acids 598-603 of SEQ ID NO:2 and 599-604 of SEQ ID NO:4);
- j) LLRFSE (amino acids 599-604 of SEQ ID NO:2 and 600-605 of SEQ ID NO:4);
- k) LRFSES (amino acids 600-605 of SEQ ID NO:2 and 601-606 of SEQ ID NO:4);
- l) RFSESS (amino acids 601-606 of SEQ ID NO:2 and 602-607 of SEQ ID NO:4);
- m) ENIPEN (amino acids 654-659 of SEQ ID NO:2 and 657-662 of SEQ ID NO:4);
- n) NIPENP (amino acids 655-660 of SEQ ID NO:2 and 658-663 of SEQ ID NO:4);

and

- o) IPENPL (amino acids 656-661 of SEQ ID NO:2 and 659-664 of SEQ ID NO:4).

73. The recombinant DNA molecule of Claim 72 wherein the sequence of contiguous amino acid residues contains seven or more consecutive amino acids and is selected from the group consisting of:

- a) GFRKFNI (amino acids 372-378 of SEQ ID NO:2 and 376-382 of SEQ ID NO:4);
- b) FRKFNIL (amino acids 373-379 of SEQ ID NO:2 and 377-383 of SEQ ID NO:4);
- c) LSWQFSS (amino acids 500-506 of SEQ ID NO:2 and 502-508 of SEQ ID NO:4);
- d) GTFLLRF (amino acids 596-602 of SEQ ID NO:2 and 597-603 of SEQ ID NO:4);
- e) TFLLRF (amino acids 597-603 of SEQ ID NO:2 and 598-604 of SEQ ID NO:4);
- f) FLLRFSE (amino acids 598-604 of SEQ ID NO:2 and 599-605 of SEQ ID NO:4);
- g) LLRFSES (amino acids 599-605 of SEQ ID NO:2 and 600-606 of SEQ ID NO:4);
- h) LRFSESS (amino acids 600-606 of SEQ ID NO:2 and 601-607 of SEQ ID NO:4);
- i) ENIPENP (amino acids 654-660 of SEQ ID NO:2 and 657-663 of SEQ ID NO:4);

and

- j) NIPENPL (amino acids 655-661 of SEQ ID NO:2 and 658-664 of SEQ ID NO:4).

74. The recombinant DNA molecule of Claim 73 wherein the sequence of contiguous amino acid residues contains eight or more consecutive amino acids and is selected from the group consisting of:

- a) GFRKFNIL (amino acids 372-379 of SEQ ID NO:2 and 376-383 of SEQ ID NO:4);
- b) GTFLLRF (amino acids 596-603 of SEQ ID NO:2 and 597-604 of SEQ ID NO:4);
- c) TFLLRFSE (amino acids 597-604 of SEQ ID NO:2 and 598-605 of SEQ ID NO:4);
- d) FLLRFSES (amino acids 598-605 of SEQ ID NO:2 and 599-606 of SEQ ID NO:4);
- e) LLRFSESS (amino acids 599-606 of SEQ ID NO:2 and 600-607 of SEQ ID NO:4);

and

- f) ENIPENPL (amino acids 654-661 of SEQ ID NO:2 and 657-664 of SEQ ID NO:4).

75. The recombinant DNA molecule of Claim 74 wherein the sequence of contiguous amino acid residues contains nine or more consecutive amino acids and is selected from the group consisting of:

- a) GTFLLRFSE (amino acids 596-604 of SEQ ID NO:2 and 597-605 of SEQ ID NO:4);

b) TFLRRFSES (amino acids 597-605 of SEQ ID NO:2 and 598-606 of SEQ ID NO:4); and

c) FLLRFSESS (amino acids 598-606 of SEQ ID NO:2 and 599-607 of SEQ ID NO:4).

76. The recombinant DNA molecule of Claim 75 wherein the sequence of contiguous amino acid residues contains ten or more consecutive amino acids and is selected from the group consisting of:

a) GTFLRRFSES (amino acids 596-605 of SEQ ID NO:2 and 597-606 of SEQ ID NO:4); and

b) TFLRRFSESS (amino acids 597-606 of SEQ ID NO:2 and 598-607 of SEQ ID NO:4).

77. The recombinant DNA molecule of Claim 76 wherein the sequence of contiguous amino acid residues contains eleven consecutive amino acids having the sequence GTFLRRFSESS (amino acids 596-606 of SEQ ID NO:2 and 597-607 of SEQ ID NO:4).

78. The recombinant DNA molecule of Claim 70 wherein said RRF has an amino acid sequence which further comprises a second sequence of contiguous amino acid residues, wherein the second sequence of contiguous amino acid residues also contains four or more consecutive amino acids which is present in both SEQ ID NO:2 and SEQ ID NO:4.

79. A recombinant DNA molecule encoding a receptor recognition factor (RRF) protein having the following characteristics:

a) said RRF is cytoplasmic in origin;

b) said RRF is activated by tyrosine phosphorylation; and

c) upon activation said RRF is translocated to the nucleus of a target cell, wherein said DNA molecule hybridizes to the nucleotide sequence set forth in SEQ ID NO:1 under standard hybridization conditions.

80. A recombinant DNA molecule encoding a receptor recognition factor (RRF) protein having the following characteristics:

- a) said RRF is cytoplasmic in origin;
- b) said RRF is activated by tyrosine phosphorylation; and
- c) upon activation said RRF is translocated to the nucleus of a target cell; wherein said DNA molecule hybridizes to the nucleotide sequence set forth in SEQ ID NO:3 under standard hybridization conditions.

81. A recombinant DNA molecule encoding a receptor recognition factor (RRF) protein having the following characteristics:

- (a) the RRF is cytoplasmic in origin;
- (b) the RRF is activated by tyrosine phosphorylation; and
- (c) upon activation said RRF is translocated to the nucleus of a target cell;

wherein the RRF contains one or more of the boxed regions in Figure 8B.

82 The recombinant DNA molecule of Claim 81, wherein the RRF further contains a tyrosyl residue at a position that corresponds to the conserved position identified in SEQ ID NO:2 and SEQ ID NO:4, said position selected from the group consisting of:

- amino acid 22 of SEQ ID NO:2 and amino acid 22 of SEQ ID NO:4;
- amino acid 34 of SEQ ID NO:2 and amino acid 33 of SEQ ID NO:4;
- amino acid 288 of SEQ ID NO:2 and amino acid 289 of SEQ ID NO:4;
- amino acid 631 of SEQ ID NO:2 and amino acid 634 of SEQ ID NO:4;
- amino acid 648 of SEQ ID NO:2 and amino acid 651 of SEQ ID NO:4;
- amino acid 665 of SEQ ID NO:2 and amino acid 668 of SEQ ID NO:4;
- amino acid 677 of SEQ ID NO:2 and amino acid 680 of SEQ ID NO:4;
- amino acid 678 of SEQ ID NO:2 and amino acid 681 of SEQ ID NO:4; and
- amino acid 690 of SEQ ID NO:2 and amino acid 701 of SEQ ID NO:4.

83. The recombinant DNA molecule of Claim 81 wherein the RRF comprises a highly negative charged domain at its C-terminal end.

84. The recombinant DNA molecule of Claim 81 wherein the RRF comprises an SH2 domain.
85. The recombinant DNA molecule of Claim 84 wherein the SH2 domain contains an arginine at a position that corresponds to amino acid 601 of SEQ ID NO:2 and amino acid 602 of SEQ ID NO:4.
86. The recombinant DNA molecule of Claim 81 wherein the RRF forms a dimer upon said activation by tyrosine phosphorylation.
87. The recombinant DNA molecule of Claim 81 wherein the activation of the RRF is unaffected by the presence or concentration of second messengers.
88. The recombinant DNA molecule of Claim 81 wherein the RRF can act as a DNA binding protein upon said activation by tyrosine phosphorylation.
89. The recombinant DNA molecule of Claim 81 wherein the RRF interacts with an interferon- $\gamma$ -bound receptor kinase complex.
90. The recombinant DNA molecule of Claim 88 wherein the RRF can stimulate ISRE-dependent or gamma activated site (GAS)-dependent transcription.
91. An isolated nucleic acid encoding a receptor recognition factor (RRF) protein having the following characteristics:
- (a) the RRF is cytoplasmic in origin;
  - (b) the RRF is activated by tyrosine phosphorylation; and
  - (c) upon activation said RRF is translocated to the nucleus of a target cell;
- wherein the RRF contains one or more of the boxed regions in Figure 8B.



92. The isolated nucleic acid of Claim 91, wherein the RRF further contains a tyrosyl residue at a position that corresponds to the conserved position identified in SEQ ID NO:2 and SEQ ID NO:4, said position selected from the group consisting of:

amino acid 22 of SEQ ID NO:2 and amino acid 22 of SEQ ID NO:4;  
amino acid 34 of SEQ ID NO:2 and amino acid 33 of SEQ ID NO:4;  
amino acid 288 of SEQ ID NO:2 and amino acid 289 of SEQ ID NO:4;  
amino acid 631 of SEQ ID NO:2 and amino acid 634 of SEQ ID NO:4;  
amino acid 648 of SEQ ID NO:2 and amino acid 651 of SEQ ID NO:4;  
amino acid 665 of SEQ ID NO:2 and amino acid 668 of SEQ ID NO:4;  
amino acid 677 of SEQ ID NO:2 and amino acid 680 of SEQ ID NO:4;  
amino acid 678 of SEQ ID NO:2 and amino acid 681 of SEQ ID NO:4; and  
amino acid 690 of SEQ ID NO:2 and amino acid 701 of SEQ ID NO:4.

93. The recombinant DNA molecule of Claim 81 that is operatively linked to an expression control sequence.

94. An expression vector containing the recombinant DNA molecule of Claim 93.

95. A method of expressing a recombinant receptor recognition factor in a cell containing the expression vector of Claim 94 comprising culturing the cell in an appropriate cell culture medium under conditions that provide for expression of the receptor recognition factor by the cell.

96. The method of Claim 95 further comprising the step of purifying the recombinant receptor recognition factor.--

#### REMARKS

The Specification has been amended to incorporate references to the appropriate SEQ ID NOs:, where specific sequences are indicated. Applicants have amended the Specification to note the status of the parent applications, above and have also addressed the issues